

United States Patent [19]

Mayer et al.

[11] Patent Number: 5,556,838

[45] Date of Patent: *Sep. 17, 1996

[54] INHIBITING THE DEVELOPMENT OF TOLERANCE TO AND/OR DEPENDENCE ON AN ADDICTIVE SUBSTANCE

[75] Inventors: David J. Mayer; Donald D. Price; Jianren Mao, all of Richmond, Va.; John W. Lyle, Belmar, N.J.

[73] Assignee: Virginia Commonwealth University, Richmond, Va.

[*] Notice: The term of this patent shall not extend beyond the expiration date of Pat. No. 5,321,012.

[21] Appl. No.: 245,970

[22] Filed: May 19, 1994

Related U.S. Application Data

[63] Continuation of Ser. No. 43,280, Apr. 6, 1993, Pat. No. 5,321,012, which is a continuation-in-part of Ser. No. 10,583, Jan. 28, 1993, abandoned.

[51] Int. Cl.⁶ A61K 31/70; A61K 31/54; A61K 31/44; A61K 31/445

[52] U.S. Cl. 514/25; 514/216; 514/223.5; 514/225.5; 514/224.5; 514/282; 514/231.2; 514/304; 514/305; 514/306; 514/307; 514/812

[58] Field of Search 514/25, 304, 305, 514/306, 307, 216, 223.5, 225.5, 224.5, 282, 231.2, 812

[56] References Cited

PUBLICATIONS

Pharmacol. Biochem. Behav. vol. 35, No. 4 (1990), pp. 829-832.

Pharmacol. Biochem. Behav. vol. 43, No. 2 (1992), pp. 487-490.

Dtsch. Apoth.-Ztg. vol. 119, No. 21 (1979), p. 821, "Opiat-Rezeptoren und Endorphine".

Truillo et al.; "Inhibition of Morphine . . . MIC801"; Science; vol. 251, pp. 84-87.

Marek et al; "Brain Research, Delayed application of MIC801 . . . in rats."; vol. 558, pp. 163-165.

Primary Examiner—Theodore J. Criares

Attorney, Agent, or Firm—Dilworth & Barrese

[57] ABSTRACT

Nontoxic substances that block the N-methyl-D-aspartate (NMDA) receptor, e.g., a morphinan such as dextromethorphan or dextrorphan, or that block a major intracellular consequence of NMDA-receptor activation, e.g., a ganglioside such as GM₁ or GT_{1b}, a phenothiazine such as trifluoperazine or a naphthalenesulfonamide such as N-(6-aminohexyl)-5-chloro-1-naphthalenesulfonamide, inhibit the development of tolerance to and/or dependence on addictive drugs, e.g., narcotic analgesics such as morphine, codeine, etc.

2 Claims, 10 Drawing Sheets